Case report: Fatal hemorrhagic disease in a newborn despite vitamin K prophylaxis

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Vitamin K prophylaxis is recommended for all neonates to prevent hemorrhagic disease of the newborn (HDN).[1] This case report describes an infant who died from complications related to HDN despite receiving a single oral dose (10 mg) of vitamin K at birth. Family physicians are reminded that giving vitamin K to neonates does not guarantee protection from development of HDN. With this case, we emphasize to family physicians the changes in recommendations for administering vitamin K.

Case description

A 7-week-old aboriginal* boy was brought to a family doctor's office because his parents perceived changes in his behaviour. His mother reported that he had stopped smiling and that he was feeding poorly. Medical history revealed an uncomplicated vaginal delivery after an unremarkable pregnancy. At birth, he was given 10 mg of vitamin K by mouth. Growth, development, and behaviour had been completely normal since birth. He was being exclusively breastfed. No abnormalities were detected on clinical examination at the doctor's office.

The following afternoon, the boy was brought to the emergency department because of vomiting, irritability, and unusual posture and stiffening. On examination, the baby was pale and slightly jaundiced, but he sucked well on a finger. During a cranial ultrasound examination, myoclonic movements suggested a generalized tonic-clonic seizure. Prolonged oozing from both heel prick and venipuncture sites was noted a couple of hours after blood collection. Laboratory results revealed normocytic, normochromatic anemia (96 g/L); thrombocytosis (650 x 10^9/L); moderate leukocytosis (15.9 x 10^9/L, and mild conjugated hyperbilirubinemia (total 93 µmol/L, direct 45 µmol/L).

An intraventricular hemorrhage in the right lateral ventricle was detected by ultrasonography. The infant was immediately transferred to a tertiary care hospital. On arrival, he was noted to have a full, tense anterior fontanel; stiff limbs; and eyes that deviated to the left. His pupils were small and nonreactive. His breathing was periodic with episodes of apnea. Seizure activity was evident. A computed tomographic scan showed a large intracerebral hemorrhage on the right side with obliteration of the right ventricle and marked swelling of the right hemisphere encroaching into the left hemisphere. Clotting studies revealed a prothrombin time (INR) of >32 and a partial thromboplastin time (PTT) of 202. His fibrinogen was 24 mg/L and his platelet count was 713, suggesting a coagulopathy involving clotting factors and not due to thrombocytopenia or disseminated intravascular coagulation.

He was given fresh frozen plasma (20 mg/kg) and intravenous vitamin K (2 mg). Eight hours later, his PT-INR had dropped to 0.9 and his PTT to 19, and oozing from peripheral sites had ceased. Vitamin K deficiency was, therefore, the working diagnosis for the coagulopathy.

The baby developed a right hemiparesis, a rock-hard anterior fontanel, and a dilated right pupil 30 hours after admission. The electroencephalogram study was flat 48 hours after admission, and ventilation was continued until all other vital signs had ceased. Autopsy confirmed the presence of an acute right occipitoparietal intracerebral hemorrhage and bilateral bronchopneumonia.

Discussion

Hemorrhagic disease of the newborn can present at any time up to 8 weeks after birth. The infant in this case report developed HDN of the late-onset type. Late HDN is more common among breastfed

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**The term aboriginal is used to describe the indigenous people of Canada and their descendents.*

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Key points

- The preferred method of vitamin K administration is by intramuscular injection within 6 hours of birth. Infants with birth weights < 1500 g should receive 0.5 mg; those weighing > 1500 g should receive 1.0 mg.
- If oral administration is chosen, infants should receive three doses of 2.0 mg: one with the first feed, one at 2 to 4 weeks, and one at 4 to 6 weeks.

neonates, presumably because human milk has much lower levels of vitamin K than infant formula does.[2-4]

Routine administration of vitamin K is an effective way to decrease the incidence of HDN. The incidence of late HDN in infants not given vitamin K prophylaxis is reported to be 4.4 to 7.1 per 100 000 births.[2,5] In 1961, the American Academy of Pediatrics recommended that all newborns be given 0.5 to 1.0 mg of vitamin K intramuscularly shortly after birth. After these recommendations were implemented, the estimated incidence rate of late HDN fell to 0.07 to 0.25 per 100 000 infants.[1,2,6]

In response to concerns about the possible psychologic effects of intramuscular injections on babies and parents and a possible increased risk of childhood cancer after intramuscular administration of vitamin K, physicians in many countries began to administer vitamin K orally rather than intramuscularly. In 1988, the Canadian Paediatric Society reviewed the literature and recommended that all neonates continue to receive a single dose of vitamin K, either 1.0 mg intramuscularly or 2.0 mg orally, within 6 hours of birth.[7] This recommendation was reviewed in 1993, and the oral dosing regimen was changed to three doses: one at birth, one at 1 to 2 weeks, and one at 4 to 6 weeks.[8] Both compliance and loss to follow up have proved to be serious problems with oral prophylaxis.[9]

The switch to oral vitamin K was associated with a resurgence of late HDN reported from countries such as Germany, Great Britain, Sweden, and Australia. Epidemiologic studies and meta-analysis of cohort studies have confirmed that the switch to oral vitamin K is associated with a small but significant increase in incidence to approximately 1.4 per 100 000 infants.

The relative risk of developing HDN after a single oral dose of vitamin K compared with a single intramuscular dose of vitamin K is estimated to be at least 8.15 (95% confidence interval 1.32 to 28.63).[1] Relative risk without prophylaxis is in the order of 81:1.[10]

The infant in this case received oral vitamin K prophylaxis postpartum but not during follow up. The single dose of vitamin K given (10 mg) was greater than the total amount recommended by the Canadian Paediatric Society.[1,8] It was apparently insufficient, however, to prevent late-onset HDN.

Conclusion

New guidelines for routine administration of vitamin K to newborns have been released recently.[1] According to these guidelines, vitamin K_1 should be given as a single intramuscular dose of 0.5 mg (birth weight ≤ 1500 g) or 1.0 mg (birth weight > 1500 g) to all newborns within 6 hours of birth. If parents refuse the intramuscular injection, physicians should recommend that infants receive an oral dose of 2.0 mg of vitamin K (use parenteral form) at the time of first feeding. The oral dose of 2.0 mg of vitamin K should be given again at 2 to 4 weeks and again at 6 to 8 weeks of age. The importance of these follow-up doses should be emphasized to parents, who should also be warned that their infants remain at increased risk of late HDN using this regimen.

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